THE EPIDEMIOLOGY OF RETINAL VEIN OCCLUSION: THE BEAVER DAM EYE STUDY*

BY *Ronald Klein, MD, Barbara E.K. Klein, MD, Scot E. Moss, MA* (BY INVITATION), AND *Stacy M. Meuer, BS* (BY INVITATION)

ABSTRACT

Purpose: To describe the prevalence and the 5-year incidence of retinal central and branch vein occlusion and associated risk factors.

Methods: The Beaver Dam Eye Study (n=4,926) is a population-based study in which retinal vein occlusions were detected at baseline (1988-1990) and at a 5-year follow-up examination (1993-1995) by grading of 30° color fundus photographs.

Results: The prevalence and 5-year incidence of retinal branch vein occlusion were each 0.6%. The prevalence of retinal central vein occlusion was 0.1%, and the 5-year incidence was 0.2%. While adjusting for age, the prevalence of branch vein occlusion was associated with hypertension (odds ratio [OR] 5.42, 95% confidence interval [CI] 2.18, 13.47), diabetes mellitus (OR 2.43, 95% CI 1.04, 5.70), pulse pressure (OR 1.24 for 10 mm Hg, 95% CI 1.03, 1.48), ocular perfusion pressure (OR 2.09 for 10 mm Hg, 95% CI 1.45, 3.01), arteriovenous nicking (OR 16.75, 95% CI 7.33, 38.24), and focal arteriolar narrowing (OR 22.86, 95% CI 8.43, 62.03). The age-adjusted incidence of retinal branch vein occlusion was associated with current smoking (OR 4.43 95%, CI 1.53, 12.84) compared with nonsmokers and to focal arteriolar narrowing (OR 5.24, 95% CI 1.97, 13.94) at baseline. While controlling for age, the incidence of branch vein occlusion was not associated with serum lipid levels, body mass index, white blood cell count, alcohol consumption, aspirin use, glaucoma, intraocular pressure, or ocular hypertension.

Conclusions: Retinal vein occlusion is infrequent in the population. These data suggest a strong association between retinal branch vein occlusion and retinal arteriolar changes. Data from larger populations are needed to further assess associations between risk factors and the incidence of retinal vein occlusions.

Tr Am Ophth Soc 2000;98:133-143

INTRODUCTION

Retinal vein occlusions are an important cause of vision loss.[1,2] Most of the information about retinal vein occlusions has come from clinical case series,[1,3-6] case-control studies,[7-13] and clinical trials.[14-16] To date, information about the prevalence of retinal branch vein occlusion has been limited.[17,18] In the population-based Blue Mountains Eye Study, the prevalence of retinal vein occlusion was 1.6%.[17] In the Framingham Eye Study, of the 2,631 persons who underwent a screening examination, 4 of the 156 eyes found to have retinopathy had a retinal vein occlusion.[18]

Data from previous studies have shown an association of retinal branch vein occlusion with hypertension, atherosclerotic vascular disease, diabetes mellitus, rheological factors, refractive error, elevated intraocular pressure, and open-angle glaucoma, although these associations have not been consistent.[6-8,10-13,17] Data from earlier studies suggest no association of retinal central vein occlusion with decreased survival.[19,20] Less is known about the relation of retinal branch vein occlusion and survival. The purposes of this report are (1) to describe the prevalence and incidence of retinal vein occlusion, (2) to examine associated risk factors, and (3) to describe the relationship of retinal vein occlusion to stroke and ischemic heart disease mortality in a large population-based cohort in Beaver Dam, Wisconsin.

METHODS AND MATERIALS

The Beaver Dam Eye Study population has been described in detail in previous reports.[21,22] Briefly, a private census of the Beaver Dam, Wisconsin, population (99% white) was performed from September 15, 1987, to May 4, 1988, to identify all residents in the city or township of Beaver Dam who were 43 to 84 years of age. Of the 5,924

*From the Department of Ophthalmology and Visual Sciences, University of Wisconsin Medical School, Madison. Supported by grant EYO6594 from the National Institutes of Health (R. Klein, B.E.K. Klein) and, in part, by a Senior Scientific Investigator Award from Research to Prevent Blindness, Inc (R. Klein).

eligible individuals, 4,926 participated in the baseline examination between March 1, 1988, and September 14, 1990. Nonparticipants consisted of 226 persons (3.8%) who had died before the examination, 18 (0.3%) who could not be located, 337 (5.7%) who permitted an interview only (of these, 61 had moved), and 417 (7.0%) who refused to participate (of these, 39 had moved). Comparisons between participants and nonparticipants at the time of the baseline examination have appeared elsewhere.[21] Tenets of the Declaration of Helsinki were followed. Informed consent was signed, and institutional human experimentation committee approval was granted.

Prior to the start of the 5-year follow-up examination on March 1, 1993, 385 (7.8%) of the participants had died. Of the 4,541 participants surviving since the baseline examination, 3,684 (81.1%) participated in the follow-up examination between March 1, 1993, and June 14, 1995.[22] Four (0.1%) of the participants could not be located, 259 (5.7%) permitted an interview only (of these, 48 had moved out of the area), 423 (9.3%) refused to participate (of these, 44 had moved out of the area), and 171 (3.8%) died during the examination period. Both the mean and median times between the baseline and 5-year follow-up examinations were 4.8 years, and the standard deviation was 0.4 years.

Comparisons between participants and nonparticipants at follow-up have been presented elsewhere.[22] Persons who were alive and did not participate in the follow-up eye examination (n=686) were older at baseline than those who did (62.7 versus 60.4 years, $P<.0001$). After adjusting for age, those who were alive during the study period and did not participate were more likely to have completed fewer years of education; to have lower income, poorer visual acuity, a history of cardiovascular disease, and a history of abstaining from alcohol; to have smoked more; to have higher serum cholesterol and higher systolic and diastolic blood pressure levels; and to be retired at baseline, when compared with persons who participated.

PROCEDURES

Similar procedures were used at both baseline and follow-up examinations and have been described in detail elsewhere.[21-26] Informed consent was obtained from each participant at the beginning of the examination. The examinations at baseline and follow-up included measuring weight, height, pulse rate, and blood pressure (using a random-zero sphygmomanometer following the Hypertension Detection and Follow-up Program protocol).[27] A standardized questionnaire, including questions on the use of hormone replacement therapy in women, was administered by the examiners. Nonfasting blood specimens were obtained from participants. Serum cholesterol,[28] high-density lipoprotein (HDL) cholesterol,[29] and blood glucose[30] levels were determined by enzymatic procedures. Hematocrit values and leukocyte counts were determined by using a Coulter counter method. Blood glycated hemoglobin was determined using affinity chromatography.[31] Stereoscopic 30° color fundus photographs centered on the disc (Diabetic Retinopathy Study[32] [DRS] standard field 1) and macula (DRS standard field 2) and a nonstereoscopic color fundus photograph temporal to but including the fovea of each eye were taken. When retinal vein occlusion or other lesions were seen outside these three fields, additional fundus photographs were taken, if feasible. For purposes of this report, the 4,856 people with a photograph of at least 1 eye gradable for retinal vein occlusion are included in the analyses.

Photographs were graded using the Wisconsin Age-Related Maculopathy grading scheme.[25,26] As part of this scheme, all photographic fields of each eye were examined by the graders to detect retinal vein occlusions. Old central retinal vein occlusions were characterized by occluded and sheathed retinal veins, while more recent occlusions were characterized by retinal edema, optic disc hyperemia or edema, scattered superficial and deep retinal hemorrhages, and venous dilation. Branch retinal vein occlusions involved a more localized area of the retina in the sector of the obstructed venule and were characterized by scattered superficial and deep retinal hemorrhages, venous dilation, intraretinal microvascular abnormalities, and occluded and sheathed retinal venules. When present, the site of the occlusion (superotemporal, inferotemporal, or outside the temporal quadrants) was recorded. In addition, the presence of the position of the retinal arteriole to retinal venule (anterior versus not anterior) closest to the site of the occlusion was also recorded. One of the authors (R. Klein) examined all the photographs of persons with questionable or definite retinal vein occlusion.

The presence of retinal microaneurysms only, blot hemorrhages only, hemorrhages and/or microaneurysms, cotton-wool spots, hard exudates, intraretinal microvascular abnormalities, venous beading, arteriovenous nicking, new vessels on the disc and elsewhere, and preretinal and vitreous hemorrhages was graded in a masked fashion using an abbreviation of the modified Airlie House classification scheme.[32] Focal arteriolar narrowing was graded using a standard photograph from the Wisconsin Age-Related Maculopathy Grading protocol,[25] in which focal narrowing of small arterioles in the posterior pole (field 2) involves a total length of 1/3 disc diameter. Arteriolar narrowing was graded as absent, questionable, less than the standard, and greater than or equal to the standard for all arterioles more than 750 μm from the disc margin in all three standard fields. When there were multiple but separate areas of focal arteriolar narrowing, the composite length of involvement was compared with the standard. For purposes of analyses, 2 categories were used: (1) absent or questionably present and (2) present. Arteriovenous nicking was graded for all arteriovenous crossings that were more than 750 µm from the disc margin in all 3 fields. Arteriovenous nicking was graded as present if there was a decrease in the diameter of the venule on both sides of the arteriole that was crossing it. The presence of other retinal disease, such as retinal arteriolar emboli and surface wrinkling retinopathy, was graded using a detailed protocol.[25,26]

When 2 eyes of a participant were discrepant regarding the presence of a lesion, the grade assigned for the participant was that of the more severely involved eye. For example, in assigning the presence of a retinal vein occlusion, if the retinal vein occlusion was present in 1 eye but not the other, the participant would be considered to have a retinal vein occlusion. When lesions could not be graded in 1 eye, and the other eye had no lesions present, the participant's information was set to missing.

Slit-lamp and retroillumination photographs of the lenses were graded using standardized systems reported previously.[33] For this report, nuclear cataract was defined as present if the photograph of the lens was graded as more opaque than standard photograph 3. For grading the severity of cortical and posterior subcapsular opacities, a grid dividing the lens into 8 sectors and a central circle was used. Cortical opacity was considered present if, on grading the retroillumination photograph, 5% or more of the lens surface area was affected; posterior subcapsular opacity was considered present if 5% or more of any of the 8 sectors or of the central circle of the surface area of the lens was involved.

Ocular perfusion pressure (OPP) in each eye was defined by the following formula: $OPP = 2/3 (D + [S-D] /3) - IOP$, where S=systolic blood pressure and D=diastolic blood pressure.[34] Myopia was defined as a refractive error, in spherical equivalent, of -0.50 diopters or less, and hyperopia was defined as a refractive error, in spherical equivalent, of +0.50 diopters or more based on an Early Treatment Diabetic Retinopathy Study refraction. Refractive error was set to "missing" when visual acuity was 20/40 or worse or when an eye was aphakic or had an intraocular lens present.

The procedures in detecting and defining glaucoma have been presented elsewhere.[35] Intraocular pressure was measured according to a standard protocol using a Goldmann applanation tonometer. Stereoscopic fundus photographs of field 1 were used for grading of optic discs and cups according to a detailed standardized protocol. A standardized history was obtained. Subjects were queried about whether they had ever been told that they had glaucoma, were taking medicines for glaucoma, or had had surgery for glaucoma.

DEFINITIONS

For purposes of this investigation, central cataract was defined as the presence of a nuclear sclerotic cataract or a posterior subcapsular cataract or cortical cataract involving 25% or more of the central circle. The presence of at least 2 of the following 3 characteristics was needed for designation of definite glaucoma: an abnormal visual field, a large (≥0.8) or asymmetric (>0.2) cup-to-disc ratio, or a high (≥22 mm Hg) intraocular pressure. A history of taking drops or having surgery for glaucoma (excluding glaucoma secondary to rubeosis irides or trauma) was considered as probable glaucoma. Both groups were included in analyses considering glaucoma.[35]

Current age was defined as age at the time of baseline examination. The mean systolic blood pressure was the average of the 2 systolic blood pressure determinations, and the mean diastolic blood pressure was the average of the 2 diastolic blood pressures. The pulse pressure was computed by taking the difference between the mean systolic and the mean diastolic blood pressures. Hypertension was defined as a mean systolic blood pressure of 160 mm Hg or greater and/or a mean diastolic blood pressure of 95 mm Hg or greater and/or a history of hypertension with use of antihypertensive medication at the time of examination. Uncontrolled hypertension was defined as systolic blood pressure of 160 mm Hg or greater or a diastolic blood pressure of 95 mm Hg or greater. Cardiovascular disease was defined as a history of angina pectoris, myocardial infarction, or stroke or current use of cardiovascular medication such as digitalis or nitroglycerin. Cigarette smoking status was defined as follows: Subjects were classified as having never smoked if they reported having smoked fewer than 100 cigarettes in their lifetime; as ex-smokers if they had smoked more than this number of cigarettes in their lifetime but had stopped smoking before the examination; and as currently smoking if they had not stopped. There were 375 people with a previous history of adult-onset diabetes mellitus, treated with either insulin, oral hypoglycemic agents, and/or diet. There were also 48 people with newly diagnosed diabetes mellitus at baseline.[36]

STATISTICAL METHODS

SAS was used for analyzing the data, including producing proportions, chi-square statistics, and logistic regression.[37] Trends in proportions across age-groups were tested for significance using the Mantel-Haenszel procedure.[38]

McNemar's test, a special case of the Cochran-Mantel-Haenszel statistic, was used to test the differences in incidence and progression rates between eyes.[39] Liang-Zeger models were used to assess relationships with data from both eyes when a risk factor was eye-specific (retinopathy, focal retinal arteriolar narrowing, and arteriovenous nicking).[40] The relation of retinal vein occlusion to overall mortality and to mortality in which ischemic heart disease and stroke were listed as causes of death was examined after age and gender adjustment using the Cox Proportional Hazards Model.[41]

RESULTS

PREVALENCE OF RETINAL VEIN OCCLUSION

The prevalence of retinal branch vein occlusion was 0.6% (31/4,822, 95% confidence interval [CI] 0.4% to 0.9%); prevalence of retinal central vein occlusion was 0.1% (7/4,822, 95% CI 0.0% to 0.3%). Bilateral involvement was not found in any participant. The prevalence of branch and central vein occlusions varied with age, and the frequencies were similar in men and women (Table I). Persons 75 years of age or older at baseline were 6.7 times (95% CI 2.2, 20.4) as likely to have retinal branch vein occlusion present as persons 43 to 54 years of age. The overall prevalence of retinal branch vein occlusion in right eyes was similar to that in left eyes (0.4% [17/4,718] versus 0.3% [14/4,718], P=.72).

The site of the branch vein occlusion involved the superotemporal quadrant in 58.1% of eyes (18/31), the inferotemporal quadrant in 29% of eyes (9/31), and outside the temporal quadrants in 12.9% of eyes (4/31). While adjusting for age, the visual acuity was poorer in eyes with retinal branch vein occlusions involving the superior temporal quadrant (45.2 versus 52.9 letters read correctly, P< .001) compared with eyes without branch or central retinal vein occlusion. There were no differences in visual acuity in eyes with branch retinal vein occlusion affecting the inferior temporal quadrant (50 versus 52.9 letters read correctly, P=.33) or the nasal quadrants (53 versus 52.9 letters read correctly, P=.99) compared with eyes without occlusions.

Retinal arterioles were found anterior to venules nearest the occlusion in 87.1% of eyes (27/31). Retinal branch vein occlusions were more common in eyes with arteriovenous nicking (8.1% versus 0.3%, P<.001) and focal arteriolar narrowing (2.9% versus 0.1%, P<.0001) than in eyes without these changes. Focal photocoagulation scars in the macular area were present in 6.5% and a combination of scatter and focal photocoagulation scars were present in 6.5% of eyes with retinal branch vein

TABLE I: THE PREVALENCE AND 5-YEAR INCIDENCE OF RETINAL BRANCH AND CENTRAL VEIN OCCLUSION IN EITHER EYE IN THE BEAVER DAM EYE STUDY.

	BRANCH RETINAL VEIN OCCLUSION				CENTRAL RETINAL VEIN OCCLUSION			
CHARACTERISTICS	NO. AT RISK	NO.	%	*P*-VALUE	NO. AT RISK	NO.	%	*P*-VALUE
Prevalence								
Age (yr)								
43-54	1,506	3	0.2	<.0001*	1,507	1	0.1	.06*
55-64	1,303	4	0.3		1,306	1	0.1	
65-74	1,252	14	1.1		1,259	2	0.2	
75+	748	10	1.3		750	3	0.4	
Sex								
Female	2,682	19	0.7	.59†	2,688	3	0.1	.71†
Male	2,127	12	0.6		2,134	4	0.2	
Overall	4,809	31	0.6	–	4,822	7	0.1	–
Incidence								
Age (yr)								
43-54	1,258	1	0.2	<.001*	1,262	0	0.0	.10*
55-64	1,043	5	0.5		1,049	2	0.2	
65-74	914	12	1.3		931	5	0.5	
75+	343	3	0.9		351	0	0.0	
Sex								
Female	2,008	12	0.6	1.0†	2,026	4	0.2	1.0†
Male	1,550	9	0.6		1,567	3	0.2	
Overall	3,558	21	0.6	–	3,593	7	0.2	–

* Mantel-Haenszel test of trend.
† Fischer exact test.

occlusion. Macular edema involving the foveal area was present in 9.7% and retinal new vessels were present in 9.7% of eyes with retinal branch vein occlusion.

The relation of cardiovascular disease and its risk factors and other ocular and systemic conditions to prevalence of retinal branch vein occlusion at baseline is presented in Table II. After adjusting for age, retinal branch vein occlusions were associated with hypertension, elevated systolic and diastolic blood pressure, pulse pressure, diabetes mellitus, ocular perfusion pressure, focal arteriolar narrowing, and arteriovenous nicking. After controlling for hypertension status, the association of arteriovenous nicking and focal arteriolar narrowing with branch retinal vein occlusion was still statistically significant (for focal retinal arteriolar narrowing, odds ratio [OR] 16.80, 95% CI 7.57, 37.26, and for arteriovenous nicking, OR 21.94, 95% CI 8.26, 58.25). While controlling for age, prevalence of retinal branch vein occlusions was not associated with smoking status; serum lipid levels; body mass index; white blood cell count; alcohol consumption; history of cancer, angina, or myocardial infarction; aspirin use; refractive error; glaucoma; intraocular pressure or ocular hypertension; or central cataract (Table II). None of the 300 women taking hormone replacement therapy at baseline had signs of retinal branch vein occlusion.

TABLE II: AGE-ADJUSTED RELATIONS OF VARIOUS CHARACTERISTICS TO THE PREVALENCE AND 5-YEAR INCIDENCE OF RETINAL BRANCH VEIN OCCLUSION IN THE BEAVER DAM EYE STUDY

	RETINAL BRANCH VEIN OCCLUSION			
	PREVALENCE		INCIDENCE	
CHARACTERISTIC	OR* (95% CI)†	*P* VALUE	OR* (95% CI)†	*P* VALUE
Systolic blood pressure, per 10 mm Hg	1.30 (1.13, 1.50)	<.001	0.84 (0.66, 1.07)	.16
Diastolic blood pressure, per 10 mm Hg	1.68 (1.23, 2.30)	.001	0.98 (0.64, 1.49)	.91
Pulse pressure, per 10 mm Hg	1.24 (1.03, 1.48)	.02	0.77 (0.57, 1.06)	.10
Serum total cholesterol, per mmol/L	1.04 (0.77, 1.42)	.78	0.94 (0.64, 1.38)	.74
Serum HDL-cholesterol, per mmol/L	0.70 (0.30, 1.64)	.42	2.00 (0.91, 4.36)	.08
Total/HDL, per 1 unit	1.04 (0.88, 1.22)	.68	0.83 (0.63, 1.10)	.20
Hematocrit, per 10%	0.78 (0.31, 1.94)	.59	0.34 (0.11, 1.02)	.05
White blood cell count, per g/L	1.01 (0.87, 1.17)	.94	0.94 (0.74, 1.19)	.60
Platelet count, per 100 g/L	0.70 (0.42, 1.18)	.18	0.95 (0.54, 1.69)	.87
Body mass index, per kg/m²	1.04 (0.97, 1.11)	.26	0.96 (0.88, 1.05)	.38
Smoking history				
Ex vs never	0.79 (0.35, 1.80)	.60	1.21 (0.40, 3.63)	.006
Current vs never	1.35 (0.51, 3.60)		4.43 (1.53, 12.84)	
Alcohol consumption, per 100 g/wk	0.42 (0.15, 1.16)	.10	1.05 (0.77, 1.44)	.76
Heavy drinking history	0.90 (0.31, 2.59)	.84	1.57 (0.52, 4.76)	.42
Aspirin use	1.09 (0.50, 2.39)	.83	0.87 (0.32, 2.40)	.79
Diabetes history	2.43 (1.04, 5.70)	.04	1.04 (0.24, 4.51)	.96
Hypertension, any	5.42 (2.18, 13.47)	<.001	0.70 (0.28, 1.77)	.45
Untreated, uncontrolled vs normotensive	6.85 (2.07, 22.69)		‡	
Treated, controlled vs normotensive	3.79 (1.38, 10.42)	<.001		
Treated, uncontrolled vs normotensive	10.24 (3.47, 30.22)			
Myocardial infarction history	0.66 (0.16, 2.80)	.57	‡	
Angina history	0.44 (0.10, 1.89)	.27	0.86 (0.20, 3.78)	.84
Cancer history	1.05 (0.40, 2.78)	.92	1.58 (0.52, 4.79)	.42
Perfusion pressure, per 10 mm Hg	2.09 (1.45, 3.02)	<.001	0.85 (0.53, 1.37)	.56
Glaucoma	1.22 (0.27, 5.44)	.79	2.43 (0.54, 10.95)	.24
Intraocular pressure, per 1 mm Hg	0.97 (0.87, 1.08)	.60	0.95 (0.83, 1.10)	.47
Ocular hypertension	0.62 (0.08, 4.61)	.63	0.91 (0.12, 6.93)	.93
Central cataract	0.85 (0.31, 2.29)	.73	0.69 (0.17, 2.84)	.58
Refractive error				
Myopic	0.18 (0.03, 0.93)		0.43 (0.09, 2.14)	
Hyperopic	0.37 (0.13, 1.03)	.09	0.60 (0.16, 2.29)	.60
Arteriolar narrowing	16.75 (7.33,38.24)	<.001	5.24 (1.97,13.94)	<.001
Arteriovenous nicking	22.86 (8.43,62.03)	<.001	‡	

* OR, = odds ratio.
† CI, = confidence interval.
‡ Model failed to converge.

INCIDENCE OF RETINAL VEIN OCCLUSION

The incidence of retinal branch vein occlusion over the 5-year period was 0.6% (21/3,558, 95% CI 0.3 to 0.8%) and of retinal central vein occlusion, 0.2% (7/3,593, 95% CI 0.1% to 0.3%). The incidences of retinal vein occlusions varied with age and were similar in men and women (Table I). The incidence of retinal branch vein occlusion was similar in right and left eyes (0.4% [13/3,504] versus 0.3% [9/3,533], respectively, P=.52). One person with a retinal branch vein occlusion in the left eye at baseline developed one in the right eye. This subject was not included as an incident case for person-specific analyses, but the right eye was included in eye-specific analyses. In 1 person, a central retinal vein occlusion developed in both eyes.

Of those eyes that developed retinal branch vein occlusion, the site of the occlusion involved the superotemporal quadrant 45.5% of the time (10/22), the inferotemporal quadrant 36.4% of the time (8/22), and the nasal quadrants 18.2% of the time (4/22). Retinal arterioles were found anterior to venules nearest the occlusion in 77.3% of eyes (17/22). Incident retinal branch vein occlusions were not more common in eyes with arteriovenous nicking (0% [0/33] versus 0.3% [22/7002], P=1.0) but were more common in eyes with focal arteriolar narrowing at baseline (1.8% [7/395)] versus 0.2% [14/6,612], P<.001) as compared with eyes without these changes.

The relation of cardiovascular disease and its risk factors and ocular and systemic conditions to the incidence of retinal branch vein occlusion is presented in Table II. While adjusting for age, the incidence of retinal branch vein occlusion was associated with a history of current smoking. In analyses using the Liang-Zeger method,[40] after controlling for age, focal retinal arteriolar narrowing was associated with the incidence of retinal branch vein occlusion (OR 5.24, 95% CI 1.97, 13.94). The association of arteriovenous nicking with retinal branch vein occlusion could not be examined because of the small numbers of subjects with these variables. While controlling for age, the incidence of retinal branch vein occlusion was not associated with hypertension, serum lipids, body mass index, white blood cell count, alcohol consumption, history of cancer or angina, aspirin use, refractive error, glaucoma, intraocular pressure, ocular hypertension, or central cataract (Table II). An odds ratio of greater than 2 for the incidence of retinal branch vein occlusion was found for glaucoma, and odds ratios of less than 0.5 were found for myopic refraction or hematocrit as ascertained at baseline. However, these relationships were not statistically significant (P>.05).

TABLE III: RELATION OF RETINAL BRANCH VEIN OCCLUSION AT BASELINE TO STROKE AND ISCHEMIC HEART DISEASE DEATHS IN THE BEAVER DAM EYE STUDY.

	Retinal Branch Vein Occlusion*	
	Absent	Present
No.	4,778	31
Person-years	33,956.7	212.7
All deaths	724	7
Deaths/1,000 person-years	21.3	32.9
Stroke deaths	90	0
Stroke deaths/1,000 person-years	2.7	0
Ischemic heart disease deaths	227	3
Ischemic heart disease deaths/1,000 person-years	6.7	14.1

* There are 15 persons with stroke-related deaths and 17 persons with ischemic heart disease–related deaths in which retinal branch vein occlusion status at baseline was not known.

RELATIONSHIP OF RETINAL BRANCH VEIN OCCLUSION TO CARDIOVASCULAR DISEASE MORTALITY AND OCULAR MORBIDITY

Of the 31 persons with retinal branch vein occlusion present at baseline, 23 were alive and examined at the 5-year follow-up. Of these, the best-corrected visual acuity had minimally decreased from 46.9 letters read correctly (approximately equivalent to 20/32 Snellen visual acuity) to 45.7 letters read correctly over the 5-year period. No incident macular edema, retinal new vessels, focal photocoagulation, or panretinal photocoagulation was found in these eyes. No eyes previously untreated with ocular pressure–lowering drugs were now receiving such medications.

From the time of the baseline examination (1988-1990) through 1996, a total of 794 persons in the cohort died. Of those in the cohort who died, 247 persons (31.1%) had ischemic heart disease and 105 (13.2%) had stroke listed as one of the causes of death on the death certificate (Table III). People with retinal branch vein occlusion present at baseline had an 8-year age- and gender-adjusted overall survival rate of 90.4% compared with an 8-year overall survival rate of 89.4% in persons who did not have retinal branch vein occlusion present. While adjusting for age and gender, persons with retinal branch vein occlusion at baseline did not have an increased risk of dying with ischemic heart disease (hazard ratio [HR] 1.18, 95% CI 0.38, 3.68) mentioned as a cause of death compared with those without retinal branch vein occlusion. No persons with retinal branch vein occlusion at baseline had stroke death mentioned on their death certificate.

COMMENTS

Most information about the frequency of retinal vein occlusion has been derived from studies of clinic populations in which patients with severe disease may be overrepresented.[1,3,4] The Beaver Dam Eye Study provides unique population-based data on the prevalence and incidence of retinal vein occlusion using standardized protocols for the recording and grading of these lesions with stereoscopic color fundus photographs.

Retinal branch vein occlusions (0.6%) and retinal central vein occlusions (0.1%) were infrequent in the population and increased with age, affecting 1.3% and 0.4%, respectively, of those 75 years of age or older. The prevalence of retinal vein occlusion (branch and central) (0.7%) in Beaver Dam was lower than that found in the Blue Mountains Eye Study (1.6%). This difference is explained, in part, by the higher frequency of older persons in the Blue Mountains study; however, age-specific prevalence in Beaver Dam in younger age-groups was also lower than in the Blue Mountains population. The reasons for these differences are not apparent. The incidence of retinal vein occlusion in Beaver Dam, 8 per 1,000 persons, is higher than that reported in an Israeli study, where the estimated 4-year incidence was 2 per 1,000 in persons 40 years of age or older.[1]

The pathogenesis of branch retinal vein occlusion is not known. Some have postulated that hypertension and atherosclerosis and its risk factors cause retinal arteriolosclerotic changes, especially at the arteriovenous crossings, resulting in retinal venule occlusion through endothelial cell damage and thrombosis.[42,43] Others have postulated that arterioslerosis resulting in arteriolar insufficiency is the underlying pathogenetic factor leading to branch retinal vein occlusion.[44,45] In Beaver Dam, strong associations of hypertension (age-adjusted OR 5.4), focal arteriolar narrowing (age-adjusted OR 16.8), and arteriovenous nicking (age-hypertension–adjusted OR 22.9) with prevalent retinal branch vein occlusion and of focal arteriolar narrowing with incident branch vein occlusion are consistent with findings from other studies.[10-12,42] In Beaver Dam, while pulse pressure, an indirect measure of atherosclerotic large-vessel disease, was associated with prevalent branch vein occlusion, there was no association of cardiovascular disease (history of myocardial infarction, angina, or stroke) or of serum lipid levels with prevalent or incident branch vein occlusion. While data from our study suggest that localized microvascular disease, as manifest by focal arteriolar narrowing and arteriovenous nicking, may be more strongly associated with branch vein occlusion than atherosclerotic macrovascular disease, data from other studies appear to support an association of atherosclerosis and retinal branch vein occlusion. In the Blue Mountains population,[17] branch vein occlusion was associated with stroke (OR 2.6) and angina (OR 1.8) but not myocardial infarction. In the Eye Disease Case Control Study,[10] in addition to hypertension (OR 3.6), a higher odds of branch retinal vein occlusion was associated with a history of cardiovascular disease, and with increased body mass index, while lower odds were associated with higher levels of alcohol consumption, higher HDL-cholesterol (but not other lipids), and vigorous physical activity.

A strong association of current cigarette smoking (OR 4.4) with incident retinal branch vein occlusion was found in Beaver Dam. This association with smoking and incident branch vein occlusion is consistent with data from some[46-48] but not other[10,17] studies. The association of incident retinal branch vein occlusion with cigarette smoking may be explained, in part, by the inflammatory stimulus of smoking,[49] although the role of inflammation in the pathogenesis of retinal branch vein occlusion is not certain.[42]

In Beaver Dam, while controlling for age, retinal branch vein occlusion was not associated with increased risk of all-cause mortality or ischemic heart disease death. To our knowledge, there are no previous reports of an association of retinal branch vein occlusion with mortality. Previous studies have demonstrated no association between retinal central vein occlusion and ischemic heart disease morbidity or mortality.[19,20]

The higher frequency of retinal branch vein occlusion found in the superotemporal quadrant compared with other quadrants and the high frequency of the retinal arteriole found lying anterior to the vein toward the vitreous cavity are consistent with earlier findings.[50-53] Some have speculated that the consistent finding of arterioles anterior to venules at arteriovenous crossing associated with branch retinal vein occlusion supports a possible mechanical obstructive role in the pathogenesis of branch retinal vein occlusions.[51] The higher frequency in the superotemporal quadrant has been attributed to a larger number of arteriovenous crossings in that quadrant[51] or possibly may be due to relative quadrantic differences in type of direct contacts of the arterioles to the venules.[54]

In Beaver Dam, the prognosis for retaining vision was good, with a decrease of only 0.8 letters over the 5-year interval in the 23 persons who had retinal branch vein occlusion at baseline. Nearly 10% of eyes with retinal branch vein occlusion had retinal new vessels present, 10% had macular edema present, and 13% had undergone photocoagulation treatment at baseline, but no eyes with retinal branch vein occlusion at baseline were found to have developed macular edema or retinal new vessels at follow-up. These data, based on a small number of eyes with retinal branch vein occlusion, suggest a good prognosis in eyes with neither proliferative retinopathy nor macular edema at baseline.

Conclusions regarding estimates of prevalence and incidence of retinal branch vein occlusion and associations described herein must be made with caution. Misclassification may have resulted from not identifying signs of retinal branch vein occlusions in eyes with minimal retinopathy in persons without diabetes or in eyes with moderate retinopathy in persons with diabetes when there was no obvious occlusion of a retinal venule in the fundus photographs. The photographs did not include all of the retinal area in which branch vein occlusion may be found. In addition, it is possible that persons with some risk factors, such as hypertension, who developed retinal branch vein occlusion were more likely to die before follow-up, possibly underestimating its association with incidence. Some of the associations found, such as that between incident branch vein occlusion and smoking, may have been due to chance, and some of the associations not found may be due to lack of power (eg, glaucoma, stroke).

SUMMARY

The retinal vein occlusions are infrequent in the general population. A strong association of retinal arteriolar disease, as manifest by focal arteriolar narrowing, was found with retinal branch vein occlusion. Data from larger populations are needed to further assess associations between risk factors and the incidence of retinal vein occlusions.

ACKNOWLEDGMENTS

We would like to thank the Beaver Dam Eye Study Scientific Advisory Board (Mary Frances Cotch, PhD, Mae Gordon, PhD, Lee Jampol, MD, Daniel Seigel, PhD, and Robert Wallace, MD), Matthew D. Davis, MD, Barbara Blodi, MD, and Larry D. Hubbard, MAT, for scientific advice, and the primary care physicians, ophthalmologists, and optometrists of Beaver Dam, Wisconsin, and their staffs for their contributions.

REFERENCES

1. David R, Zangwill L, Bardarna M, et al. Epidemiology of retinal vein occlusion and its association with glacuoma and increased intraocular pressure. *Ophthalmologica* 1988;197:69-74.
2. Klein R, Wang Q, Klein BE, et al. The relationship of age-related maculopathy, cataract, and glaucoma to visual acuity. *Invest Ophthalmol Vis Sci* 1995;36:182-191.
3. Dodson PM, Kritzinger EE, Clough CG. Diabetes mellitus and retinal vein occlusion in patients of Asian, West Indian, and white European origin. *Eye* 1992;6:66-68
4. Hayreh SS, Zimmerman MB, Podhajsky P. Incidence of various types of retinal vein occlusion and their recurrence and demographic characteristics. *Am J Ophthalmol* 1994;117:429-441
5. Staurenghi G, Lonati C, Aschero M, et al. Arteriovenous crossing as a risk factor in branch retinal vein occlusion. *Am J Ophthalmol* 1994;117:211-213.
6. Glacet-Bernard A, Coscas G, Chabanel A, et al. Prognostic factors for retinal vein occlusion: A prospective study of 175 cases. *Ophthalmology* 1996;103:551-560.
7. Peduzzi M, Debbia A, Guerrieri F, et al. Abnormal blood rheology in retinal vein occlusion. *Graefes Arch Ophthalmol* 1986;83-85.
8. McGrath MA, Wechsler F, Hunyor ABL, et al. Systemic factors contributory to retinal vein occlusion. *Arch Intern Med* 1978;138:216-220.
9. Feist RM, Ticho BH, Shapiro MJ, et al. Branch retinal vein occlusion and quadratic variation in arteriovenous crossings. *Am J Ophthalmol* 1992;113:664-668.
10. Anonymous. Risk factors for branch retinal vein occlusion. The Eye Disease Case-Control Study. *Am J Ophthalmol* 1993;116:286-296.
11. Johnston RL, Brucker AJ, Steinmann W, et al. Risk factors of branch retinal vein occlusion. *Arch Ophthalmol* 1985;103:1831-1832.
12. Rath EZ, Frank RN, Shin DH, et al. Risk factors for retinal vein occlusions: A case-control study. *Ophthalmology* 1992;99:509-514.
13. Sperduto RD, Hiller R, Chew E, et al. Risk factors for hemiretinal vein occlusion: Comparison with risk factors for central and branch retinal vein occlusion. The Eye Disease Case-Control Study. *Ophthalmology* 1998;105:765-771.
14. Laatikainen L, Kohner EM, Khoury D, et al. Panretinal photocoagulation in central retinal vein occlusion: A randomised controlled clinical study. *Br J Ophthalmol* 1977;71:741-753.
15. Anonymous. A randomized clinical trial of early panretinal photocoagulation for ischemic central vein occlusion: The Central Retinal Vein Occlusion Study Group report. *Ophthalmology* 1995;102:1434-1444.
16. Anonymous. Argon laser scatter photocoagulation for prevention of neovascularization and vitreous hemorrhage in branch vein occlusion. A randomized clinical trial. Branch Vein Occlusion Study Group. *Arch Ophthalmol* 1986;104:34-41.
17. Mitchell P, Smith W, Chang A. Prevalence and associations of retinal vein occlusion in Australia. The Blue Mountains Eye Study. *Arch Ophthalmol* 1996;114:1243-1247.
18. Leibowitz HM, Krueger DE, Maunder LR, et al. The Framingham Eye Study monograph: An ophthalmological and epidemiological study of cataract, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2,631 adults, 1973-1975. *Surv Ophthalmol* 1980;24:335-610.
19. Elman MJ, Bhatt AK, Quinlan PM, et al. The risk for systemic vascular diseases and mortality in patients with central retinal vein occlusion. *Ophthalmology* 1990;97:1543-1548.
20. Mansour AM, Walsh JB, Henkind P. Mortality and morbidity in patients with central retinal vein occlusion. *Ophthalmologica* 1992;204:199-203.
21. Klein R, Klein BEK, Linton KLP, et al. The Beaver Dam Eye Study: Visual acuity. *Ophthalmology* 1991;98:1310-1315.
22. Klein R, Klein BEK, Lee KE. Changes in visual acuity in a population. The Beaver Dam Eye Study. *Ophthalmology* 1996;103:1169-1178.
23. Klein R, Klein BEK. *The Beaver Dam Eye Study. Manual of Operations*. Springfield, Va: US Department of Commerce; 1991. NTIS Accession No. PB 91-149823.
24. Klein R, Klein BEK. *The Beaver Dam Eye Study II. Manual of Operations*. Springfield, Va: US Department of Commerce; 1995. NTIS Accession No. PB 95-273827.
25. Klein R, Davis MD, Magli YL, et al. *Wisconsin Age-Related Maculopathy Grading System*. Springfield, Va: US Department of Commerce; 1991. NTIS Accession No. PB 91-184267.
26. Klein R, Davis MD, Magli YL, et al. The Wisconsin age-related maculopathy grading system. *Ophthalmology* 1991;98:1128-1134.
27. Anonymous. The Hypertension Detection and Follow-up Program: Hypertension Detection And Follow-up Program Cooperative Group. *Prev Med* 1976;5:207-215.
28. Allain CC, Poon LS, Chan CS, et al. Enzymatic determination of total serum cholesterol. *Clin Chem* 1974;20:470-475.
29. Lopes-Virella MF, Stone P, Ellis S, et al. Cholesterol determination in high-density lipoproteins separated by three different methods. *Clin Chem* 1977;23:882-884.

30. Stein MW. D-glucose determination with hexokinase and glucose-6-phosphate dehydrogenase. In: Bergmeyer HC, ed. *Methods of Enzymatic Analysis*. New York: Academic Press; 1963:177.
31. Klenk DC, Hermanson GT, Krohn RI, et al. Determination of glycosylated hemoglobin by affinity chromatography: Comparison with colorimetric and ion-exchange methods, and effects of common interferences. *Clin Chem* 1982;28:2088-2094.
32. Anonymous. Early Treatment Diabetic Retinopathy Study design and baseline patient characteristics. ETDRS Report No. 7. *Ophthalmology* 1991;98:741-756.
33. Klein BEK, Klein R, Linton KLP, et al. Assessment of cataracts from photographs in the Beaver Dam Eye Study. *Ophthalmology* 1990;97:1428-1433.
34. Moss SE, Klein R, Klein BEK. Ocular factors in the incidence and progression of diabetic retinopathy. *Ophthalmology* 1994;101:77-83.
35. Klein BEK, Klein R, Sponsel WE, et al. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology* 1992;99:1499-1504.
36. Klein R, Klein BEK, Moss SE, et al. The Beaver Dam Eye Study. Retinopathy in adults with newly discovered and previously diagnosed diabetes mellitus. *Ophthalmology* 1992;99:58-62.
37. SAS Institute. SAS User's Guide: Statistics, Version 6 Edition. Cary, NC: SAS Institute; 1990.
38. Mantel N. Chi-square tests with one degree of freedom: Extensions of the Mantel-Haenszel procedure. *J Am Stat Assoc* 1963;58:690-700.
39. Agresti A. *Categorical Data Analysis*. New York: John Wiley & Sons; 1990:349-350.
40. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986;73:13-22.
41. Cox DR. Regression models and life-tables (with discussion). *J R Stat Soc Ser B* 1972;182-220.
42. Williamson TH. Central retinal vein occlusion: What's the story? *Br J Ophthalmol* 1997;871:698-704.
43. Frangieh GT, Green WR, Barraquer-Somers E, et al. Histopathologic study of nine branch retinal vein occlusions. *Arch Ophthalmol* 1982;100:1132-1140.
44. Rabinowicz IM, Litman S, Michaelson IC. Branch venous thrombosis: A pathological report. *Trans Ophthalmol Soc U K* 1969;88:191-210.
45. Paton A, Rubinstein K, Smith VH. Arterial insufficiency in retinal venous occlusion. *Trans Ophthalmol Soc U K* 1964;84:559-595.
46. Dodson PM, Galton DJ, Hamilton AM, et al. Retinal vein occlusion and the prevalence of lipoprotein abnormalities. *Br J Ophthalmol* 1982;66:161-164.
47. Dodson PM, Kritzinger EE. Management of retinal vein occlusion. *Br Med J* 1987;295:1434-1435.
48. Ellis CJ, Hamer DB, Hunt RW, et al. Medical investigation of retinal vascular occlusion. *Br Med J* 1964;ii:1093-1098.
49. Friedman GD, Siegelaub AB, Seltzer CC, et al. Smoking habits and the leukocyte count. *Arch Environ Health* 1973;26:137-143.
50. Feist RM, Ticho BH, Shapiro MJ, et al. Branch retinal vein occlusion and quadratic variation in arteriovenous crossings. *Am J Ophthalmol* 1992;113:664-668.
51. Zhao J, Sastry SM, Sperduto RD, et al. Arteriovenous crossing patterns in branch retinal vein occlusion: The Eye Disease Case-Control Study Group. *Ophthalmology* 1993;100:423-428.
52. Duker JS, Brown GC. Anterior location of the crossing artery in branch retinal vein obstruction. *Arch Ophthalmol* 1989;107:998-1000.
53. Staurenghi G, Lonati C, Aschero M, et al. Arteriovenous crossing as a risk factor in branch retinal vein occlusion. *Am J Ophthalmol* 1994;117:211-213.
54. Michaelson IC. *Textbook of the Fundus of the Eye*. 3rd ed. Edinburgh: Churchill Livingstone; 1980:78-80.

DISCUSSION

Dr Froncie A. Gutman. The Beaver Dam Eye Study (BDES) is a large population (n=4926) based study of persons 43 to 86 years of age. This study on the epidemiology of retinal vein occlusion (RVO) reports a low prevalence and incidence of retinal vein occlusion, the associated risk factors for branch retinal vein occlusion (BRVO), and the lack of a relationship between BRVO and mortality in patients with ischemic heart disease and stroke. With respect to BRVO, the prevalence was 0.6% (31/4822) and the incidence was 0.6% (21/3558). For central retinal vein occlusion (CRVO), the prevalence was 0.1% (7/4822) and the incidence was 0.2% (7/3593). As the authors have properly noted, the low prevalence and incidence of RVO limits the statistical power of this study. Hypertension, ocular perfusion pressure and diabetes mellitus were 3 of the risk factors for prevalence of BRVO. Current smoking was an associated risk factor for the incidence of BRVO. Because of the few eyes with CRVO, no statistically valid data was available on risk factors for CRVO.

My first concern is that the prevalence and incidence of retinal vein occlusion was based solely upon a reading center's review of retinal color photographs taken 5 years apart. The baseline examinations were performed in 1988-1990 and the subsequent follow-up evaluations were obtained 5 years later, between 1993-1995. Retinal photographs which focused on the disk macula and mid-peripheral temporal retina provided an incomplete survey of the retina. No comment is made about substandard photographs due to technical problems or media opacities. In this study, no patient received a dilated retinal examination by an ophthalmologist. It is of interest that the Blue Mountains Eye Study, which reported a much higher prevalence of RVO, included a retinal examination by an ophthalmologist.

Although ischemic retinal vein occlusions commonly produce a chronic visible change in the retina (i.e., sheathed retinal vessels, retinal hemorrhages, neovascularization, retinal pigment epithelial disturbance, etc.), the more common perfused RVO, which comprise approximately 75% of all RVOS, is less likely to do so. Forty percent of perfused RVO's can have a remission of the clinical signs of venous occlusive retinopathy within 6-14 months. In eyes undergoing a partial remission of a perfused RVO, the residual retinopathy may resemble diabetic retinopathy with localized microaneurysms, with or without exudates, and with or without macular edema. In eyes with localized or diffuse microangiopathy of undetermined etiology, a fluorescein angiogram is very helpful in identifying the characteristic angiographic patterns and signs of a prior BRVO or CRVO. Fluorescein angiography was not included in the study protocol. The 5 year interval between retinal photographs in this study provides more than adequate time for the occurrence and remission of a RVO. Without visible signs of a past RVO being evident in the color photographs, this study suffers the liability of underestimating the prevalence and the incidence RVO.

My second observation concerns the racial profile of this study population. Ninety-nine percent of the participants were white. This study, as well as other studies, has documented age, hypertension and diabetes as increasing the risk for BRVO. When compared to a white population, African Americans have a higher prevalence of hypertension and a greater rate of more severe hypertension which is accompanied by an 80% higher stroke mortality rate, and a 50% higher heart disease mortality rate. In addition, African Americans and Hispanics have a higher prevalence of diabetes mellitus (1,2,3). The lack of a racially balanced study population would bias this study's results towards a lower prevalence and incidence of RVO compared to a racially balanced study population.

The third observation concerns the loss of approximately 20% of the study population for the 5-year follow-up examination (4,926 vs 3,684). 7.8% or 385 study patients had died. Although death is an uncontrollable variable in any longitudinal epidemiological study, did the total of 1242 study patients who were either dead or lost to follow-up, have a greater risk profile for the development of BRVO? If they did have a high risk profile, (older age, hypertension, diabetes) this could bias the study towards a lower incidence of RVO and might alter the statistical analyses of associated risk factors.

I have 3 questions for the authors:

1. What factors do you believe caused the Blue Mountains Eye Study to report a prevalence rate for retinal vein occlusion which was almost 270% higher than the rate in your study (0.6% vs 1.6%)?

2. Did the patients who died or were lost to follow-up have a high risk profile for development of RVO such as older age, hypertension and diabetes?

3. Were there any eyes that could not be evaluated because of poor quality retinal photographs? If this occurred, how many eyes could not be evaluated?

REFERENCES

1. NIH, National Institute of Diabetes and Digestive and Kidney Diseases, Diabetes in America, 2nd Edition, NIH Publication No. 95-1468, 1995;613-659.
2. Hypertension, 1995;Vol. 26:1,60-69.
3. NIH, National Institute of Heart, Lung, and Blood, High Blood Pressure, NIH Publication No 98-4080, 1997;41-53.

Dr Frederick L. Ferris. I congratulate Ron on a very nice paper and summary of vein occlusion in a population. In view of the risk factors for retinal vein occlusion, I was surprised that there wasn't an increased mortality in these patients. Will you discuss the confidence intervals around this apparent negative association, particularly in relation to the small sample size of this group of patients?

Dr Ronald Klein I want to thank Dr Froncie Gutman for his thoughtful comments regarding my paper. I also wanted to thank him for sharing his clinical insights regarding the natural history of branch retinal vein occlusions in a series of telephone conversations I had with him over the past few months. Dr Gutman is correct in saying that a population-based study that uses fundus photography to ascertain the presence of branch retinal vein occlusion at 2 examinations 5 years apart would underestimate both the prevalence and incidence of this condition compared to examinations using fluorescein angiography that were done more frequently. However, the latter is not feasible in a population-based cohort study.

Dr Gutman asks 3 questions. First, he asked, "What factors demonstrate the prevalence being nearly 270% greater in the Blue Mountains Eye Study?" We were fortunate in having Professor Paul Mitchell of Sydney, Australia, the Principal Investigator of the Blue Mountains Eye Study, visit us in Madison in January of this year. We presented him with a series of fundus photographs, some including eyes which we had classified as "questionable" for the presence of branch retinal vein occlusions and asked how he would classify them. He tended to classify some of these eyes, most of which had small retinal telangiectatic vessels, as having definite retinal branch vein occlusions whereas we had classified them as being questionable. In my clinical experience, in the absence of any other retinal venous changes or signs of other retinopathy, that without fluorescein angiography, it is difficult to correctly classify these eyes. A second possible reason for differences in reported age-specific rates between the Beaver Dam Eye and Blue Mountain Eye studies may be differences in the rates of hypertension, cardiovascular disease, and diabetes, conditions associated with branch retinal vein occlusion, in these populations.

The second question asked by Dr Gutman was "Is patient loss to follow-up more or less profiled by high-risk patients?" Yes. As noted in our paper, after adjusting for age, those who were alive during the study and did not participate were more likely to have a history of cardiovascular disease, to have smoked more, and to have higher systolic and diastolic blood pressures at baseline than persons who participated, The third question Dr Gutman asked was "What percentage of our fundus photograph could not be graded?" Only about 2% of participants had photographs of both eyes that could not be graded for retinal disease.

Dr Rick Ferris asked about the large confidence intervals around the estimated hazard ratio for cardiovascular disease mortality in persons with a retinal branch vein occlusion. Although we found an 18% increased risk of mortality in persons with retinal branch vein occlusion, the confidence intervals were large (0.38 to 3.68) and included an odds ratio of one, showing that the association was not significant. For infrequent conditions such as branch retinal vein occlusion, there is a need to combine data from other large population-based studies such as the Blue Mountain Eye Study and the Rotterdam study, to get a large enough sample size to achieve better estimates of this association as well as have enough statistical power to evaluate associations of other risk factors with branch retinal vein occlusion.